Proceeding as in Example 2, but substituting 2-[3-(2,4-dimethoxy-phenyl)-acryloyl]-3-hydroxy-cyclohex-2-enone for 3-[3-(2,4-dimethoxy-phenyl)-acryloyl]-4-hydroxy-6-methyl-pyran-2-one, provided 2-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone (Compound 39); MS M^+ 361.8.

Proceeding as in Example 2, but substituting benzene-1,2-diamine for 2-aminoethanethiol, provided 3-[4-(2,4-dimethoxy-phenyl)-4,5-dihydro-3*H*-benzo[*b*][1,4]diazepin-2-yl]-4-hydroxy-6-methyl-pyran-2-one (Compound 40); LCMS: MH^+ 407.2.

Proceeding as in Example 2, but substituting 3-[(E)-3-(4-dimethylamino-phenyl)-acryloyl]-4-hydroxy-6-methyl-pyran-2-one for 4-hydroxy-3-[(E)-3-(2-methoxy-4-methylsulfanyl-phenyl)-acryloyl]-6-methyl-pyran-2-one, provided 3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one (Compound 42); MS M^+ 359.0.

Proceeding as in Example 2, but substituting 3-[(E)-3-(2,4-dimethoxy-phenyl)-acryloyl]-4-hydroxy-1*H*-quinolin-2-one for 3-[3-(2,4-dimethoxy-phenyl)-acryloyl]-4-hydroxy-6-methyl-pyran-2-one, provided 3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-1*H*-quinolin-2-one (Compound 43); MS M^+ 411.0.

Proceeding as in Example 2, but substituting 4-hydroxy-6-methyl-3-[(E)-3-(4-trifluoromethoxy-phenyl)-acryloyl]-pyran-2-one for 4-hydroxy-3-[(E)-3-(2-methoxy-4-methylsulfanyl-phenyl)-acryloyl]-6-methyl-pyran-2-one, provided 4-hydroxy-6-methyl-3-[7-(4-trifluoromethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one (Compound 44); MS M^+ 399.8.

Proceeding as in Example 2, but substituting 3-[(E)-3-(bis-trifluoromethyl-phenyl)-acryloyl]-4-hydroxy-6-methyl-pyran-2-one for 4-hydroxy-3-[(E)-3-(2-methoxy-4-methylsulfanyl-phenyl)-acryloyl]-6-methyl-pyran-2-one, provided 3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one (Compound 45); MS M^+ 452.0.

Proceeding as in Example 2, but substituting 3-[(E)-3-(4-dimethylamino-2-methoxy-phenyl)-acryloyl]-4-hydroxy-6-methyl-pyran-2-one for 4-hydroxy-3-[(E)-3-(2-methoxy-4-methylsulfanyl-phenyl)-acryloyl]-6-methyl-pyran-2-one, provided 3-[7-(4-dimethylamino-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one (Compound 46); MS M^+ 389.0.

Proceeding as in Example 2, but substituting 4-hydroxy-3-[(E)-3-(4-methanesulfonyl-phenyl)-acryloyl]-6-methyl-pyran-2-one for 4-hydroxy-3-[(E)-3-(2-methoxy-4-methylsulfanyl-phenyl)-acryloyl]-6-methyl-pyran-2-one, provided 4-hydroxy-3-[7-(4-methanesulfonyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one (Compound 47); MS M^+ 393.8.

Proceeding as in Example 2, but substituting 3-[(E)-3-(2,4-diethoxy-phenyl)-acryloyl]-4-hydroxy-6-methyl-pyran-2-one for 4-hydroxy-3-[(E)-3-(2-methoxy-4-methylsulfanyl-phenyl)-acryloyl]-6-methyl-pyran-2-one and 2-amino-benzenethiol for 2-aminoethanethiol, provided 3-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-4-hydroxy-6-methyl-pyran-2-one (Compound 48); MS M^+ 452.0.

Proceeding as in Example 2, but substituting 3-[(E)-3-(2,4-diethoxy-phenyl)-acryloyl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one for 4-hydroxy-3-[(E)-3-(2-methoxy-4-methylsulfanyl-phenyl)-acryloyl]-6-methyl-pyran-2-one, provided 3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one (Compound 49); MS M^+ 406.2.

Proceeding as in Example 2, but substituting 3-[(E)-3-(4-dimethylamino-phenyl)-acryloyl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one for 4-hydroxy-3-[(E)-3-(2-methoxy-4-methylsulfanyl-phenyl)-acryloyl]-6-methyl-pyran-2-one, provided 3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one (Compound 50); MS M^+ 361.0.

Proceeding as in Example 2, but substituting 2-[(E)-3-(2,4-diethoxy-phenyl)-acryloyl]-3-hydroxy-cyclohex-2-enone for 4-hydroxy-3-[(E)-3-(2-methoxy-4-methylsulfanyl-phenyl)-acryloyl]-6-methyl-pyran-2-one, provided 2-

[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone (Compound 51); MS M^+ 390.0.

Proceeding as in Example 2, but substituting 3-hydroxy-2-[(E)-3-(2,3,4-trimethoxy-phenyl)-acryloyl]-cyclohex-2-enone for 4-hydroxy-3-[(E)-3-(2-methoxy-4-methylsulfanyl-phenyl)-acryloyl]-6-methyl-pyran-2-one, provided 3-hydroxy-2-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-cyclohex-2-enone (Compound 52); MS M^+ 392.2.

Proceeding as in Example 2, but substituting 2-[(E)-3-(2,4-diethoxy-phenyl)-acryloyl]-3-hydroxy-cyclohex-2-enone for 4-hydroxy-3-[(E)-3-(2-methoxy-4-methylsulfanyl-phenyl)-acryloyl]-6-methyl-pyran-2-one and 2-amino-benzenethiol for 2-aminoethanethiol, provided 2-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-3-hydroxy-cyclohex-2-enone (Compound 53); MS M^+ 438.4.

Proceeding as in Example 2, but substituting 3-hydroxy-2-[(E)-3-(2,3,4-trimethoxy-phenyl)-acryloyl]-cyclohex-2-enone for 4-hydroxy-3-[(E)-3-(2-methoxy-4-methylsulfanyl-phenyl)-acryloyl]-6-methyl-pyran-2-one and 2-amino-benzenethiol for 2-aminoethanethiol, provided 3-hydroxy-2-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone (Compound 54); MS M^+ 439.8.

Proceeding as in Example 2, but substituting 3-[3-(2,4-dimethoxy-phenyl)-acryloyl]-4-hydroxy-6-methyl-pyran-2-one for 4-hydroxy-3-[(E)-3-(2-methoxy-4-methylsulfanyl-phenyl)-acryloyl]-6-methyl-pyran-2-one and 2-amino-3-mercapto-3-methyl-butyric acid for 2-aminoethanethiol, provided 7-(2,4-dimethoxy-phenyl)-5-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2,2-dimethyl-2,3,6,7-tetrahydro-[1,4]thiazepine-3-carboxylic acid (Compound 55); MS M^+ 448.0.

Proceeding as in Example 2, but 4-hydroxy-6-methyl-3-[(E)-3-(2,3,4-trimethoxy-phenyl)-acryloyl]-5,6-dihydro-pyran-2-one substituted for 4-hydroxy-3-[(E)-3-(2-methoxy-4-methylsulfanyl-phenyl)-acryloyl]-6-methyl-pyran-2-one and 2-amino-benzenethiol for 2-aminoethanethiol, provided 4-hydroxy-6-methyl-

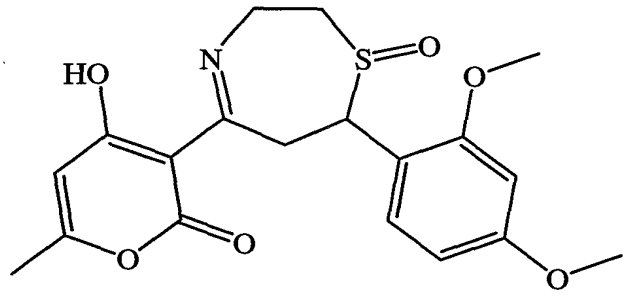
3-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-5,6-dihydro-pyran-2-one (Compound 56); MS M^+ 456.2.

Proceeding as in Example 2, but substituting 4-hydroxy-6-methyl-3-[(E)-3-(2,3,4-trimethoxy-phenyl)-acryloyl]-5,6-dihydro-pyran-2-one for 4-hydroxy-3-[(E)-3-(2-methoxy-4-methylsulfanyl-phenyl)-acryloyl]-6-methyl-pyran-2-one, provided 4-hydroxy-6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-5,6-dihydro-pyran-2-one (Compound 57); MS M^+ 408.4.

EXAMPLE 3

3-[7-(2,4-Dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1*H*-1λ^4-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one

(Compound 58)

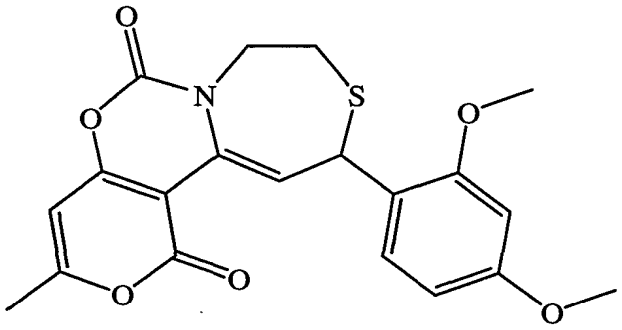


3-[7-(2,4-Dimethoxyphenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one (0.12 g, 0.32 mmol), prepared as in Reference 5, was dissolved in acetic acid (2 mL) and then hydrogen peroxide (0.3 ml, 35 wt % in water) was added at room temperature. The reaction was monitored by analytical HPLC. After 2 hours the solvent was removed *in vacuo*. Product was purified by preparative HPLC (RPC_{18} column, 2-60 % acetonitrile/water containing 0.1% HCl) to provide a diasteromeric mixture of 3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1*H*-1λ^4-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one (4.4 mg) as a yellow powder. LCMS: MH^+ 392.0.

EXAMPLE 4

10-(2,4-Dimethoxy-phenyl)-3-methyl-7,8-dihydro-10H-2,5-dioxa-9-thia-6a-aza-cyclohepta[a]naphthalene-1,6-dione

(Compound 59)

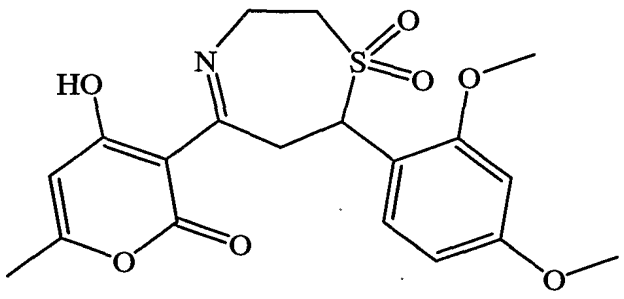


3-[7-(2,4-Dimethoxyphenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one (63 mg, 0.168 mmol), prepared as in Reference 5, was dissolved in ethylene dichloride (2 mL) and then 4-(dimethylamino)pyridine (0.020 g), di-*iso*-propylethylamine (0.5 mL) and phosgene (0.4 ml, 2 M in toluene) were added at room temperature. The reaction was monitored by analytical HPLC. After stirring at room temperature for 30 minutes, the solvent was removed *in vacuo*. Product was purified by HPLC (RPC_{18} column, 2-70 % acetonitrile/water containing 0.1% HCl) to provide 10-(2,4-dimethoxy-phenyl)-3-methyl-7,8-dihydro-10*H*-2,5-dioxa-9-thia-6a-aza-cyclohepta[*a*]naphthalene-1,6-dione (20 mg) as an off-white powder. LCMS: M^+ 401.0.

EXAMPLE 5

3-[7-(2,4-Dimethoxy-phenyl)-1,1-dioxo-2,3,6,7-tetrahydro-1H-1λ^6[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one

(Compound 60)

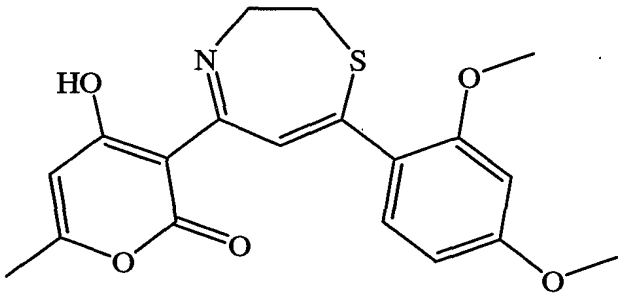


3-[7-(2,4-Dimethoxyphenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one (190 mg, 0.5 mmol), prepared as in Reference 5, was dissolved in acetic acid (2 ml) and hydrogen peroxide (0.3 ml, 35 wt % in water) was added to the solution at room temperature. The clear solution was stirred at 70°C. The reaction was monitored by analytical HPLC. After 2 hours the solvent was removed *in vacuo*. Product was purified by preparative HPLC (RPC_{18} column, 2-60 % acetonitrile/water containing 0.1% HCl) to provide 3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3,6,7-tetrahydro-1*H*-1λ^6[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one (10 mg) as a yellow powder. LCMS: MH^+ 408.0.

EXAMPLE 6

3-[7-(2,4-Dimethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one

(Compound 61)



3-[7-(2,4-Dimethoxyphenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one (150 mg, 0.39 mmol), prepared as in Reference 5, was dissolved in toluene (2 ml) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (0.3 mL, 35 wt % in water) was added to the solution. The mixture was stirred at 80°C. The reaction was monitored by analytical HPLC and after reaction was complete (20 minutes) the solvent was then removed *in vacuo*. Product was purified by preparative HPLC (RPC_{18} column, 2-80 % acetonitrile/water containing 0.1% HCl) to provide 3-[7-(2,4-dimethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one (35 mg) as an orange powder. LCMS: MH^+ 373.0.

Proceeding as in Example 6, but substituting 3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one for 3-[7-(2,4-dimethoxyphenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one, provided 3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one (Compound 62); MS M^+ 402.0.

Proceeding as in Example 6, but substituting 3-(7-[2,2']bithienyl-5-yl-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one for 3-[7-(2,4-dimethoxyphenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one, provided 3-(7-[2,2']bithienyl-5-yl-2,3-dihydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one (Compound 63); MS M^+ 402.2.

Proceeding as in Example 6, but substituting 2-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone for 3-[7-(2,4-dimethoxyphenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one, provided 2-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone (Compound 64); MS M^+ 388.4.

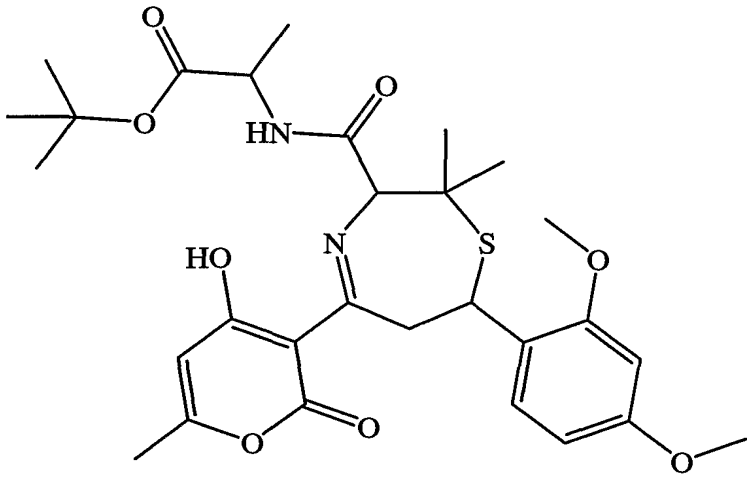
Proceeding as in Example 6, but substituting 3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one for 3-[7-(2,4-dimethoxyphenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-

hydroxy-6-methyl-pyran-2-one, provided 3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one (Compound 65); MS M^+ 404.4.

EXAMPLE 7

2-({1-[7-(2,4-Dimethoxy-phenyl)-5-(4-hydroxy-6-methyl-2-oxo-2H-pyran-3-yl)-2,2-dimethyl-2,3,6,7-tetrahydro-[1,4]thiazepin-3-yl]-methanoyl}-amino)-propionic acid tert-butyl ester

(Compound 66)



7-(2,4-Dimethoxy-phenyl)-5-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2,2-dimethyl-2,3,6,7-tetrahydro-[1,4]thiazepine-3-carboxylic acid (0.03 g), prepared as in Example 2, was dissolved in DMF (2 mL) and 2-amino-propionic acid *tert*-butyl ester (0.012 g), *N*-methylmorpholine (0.2 ml) and PyBOP (0.034 g) were added to the solution at room temperature. The mixture was stirred while the progress of the reaction was followed by analytical HPLC and when complete (16 hours) the solvent was removed *in vacuo*. Purification of product by preparative HPLC (RPC_{18} column, 2-70 % acetonitrile/water containing 0.1% HCl) provided 2-({1-[7-(2,4-dimethoxy-phenyl)-5-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2,2-dimethyl-2,3,6,7-tetrahydro-[1,4]thiazepin-3-yl]-methanoyl}-

amino)-propionic acid *tert*-butyl ester (18 mg) as an off-white powder. LCMS: M^+ 575.0.

Proceeding by methods analogous to those described in the application the following compounds can be made:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one (Compound 70),

3-[7-(4-ethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one (Compound 71),

4-hydroxy-3-[7-(3-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one (Compound 72),

3-[7-(2-bromo-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one (Compound 74),

3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one (Compound 79),

3-[7-(2,3-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one (Compound 82),

4-hydroxy-6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one (Compound 83),

4-hydroxy-6-methyl-3-(2-*p*-tolyl-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl)-pyran-2-one (Compound 85) and

4-hydroxy-6-methyl-3-[2-(4-methylsulfanyl-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-pyran-2-one (Compound 86).

EXAMPLE 8

Identification of Caspase Cascade Activators and Inducers of Apoptosis in Solid Tumor Cells

Human breast cancer cell lines T-47D and ZR-75-1 were grown according to media component mixtures designated by American Type Culture Collection + 10% fetal calf sera (FCS) (Life Technologies, Inc.) in a 5% CO_2-95% humidity

incubator as 37 °C. The T-47 and ZR-75-1 cells were maintained at a cell density between 30 and 80% confluency at a cell density of 0.1 to 0.6 x 10^6 cells/mL. Cells were harvested at 600xg and resuspended at 0.65 x 10^6 cells/mL into appropriate media + 10% FCS. An aliquot of 45 µL of cells was added to a well of a 96-well microtiter plate containing 5 µL of a 10% DMSO in RPMI-1640 media solution containing 1.6 to 100 µM of test compound (0.16 to 10 µM final). An aliquot of 45 µL of cells was added to a well of a 96-well microtiter plate containing 5 µL of a 10% DMSO in RPMI-1640 media solution without test compound as the control sample. The samples were mixed by agitation and then incubated at 37 °C for 24 hours in a 5% CO_2-95% humidity incubator. After incubation, the samples were removed from the incubator and 50 µL of a solution containing 20 µL of *N*-(Ac-DEVD)-*N*'-ethoxycarbonyl-R110 (SEQ ID NO:1) fluorogenic substrate (Cytovia, Inc.; WO99/18856), 20% sucrose (Sigma), 20 mM dithiothreitol (DTT) (Sigma), 200 mM NaCl (Sigma), 40 mM Na piperazine-*N*,*N*'-bis[2-ethanesulfonic acid] (PIPES) buffer pH 7.2 (Sigma), and 500 µg/mL lysolecithin (Calbiochem) was added. The samples were mixed by agitation and incubated at room temperature. Using a fluorescent plate reader (Model 1420 Wallac Instruments), an initial reading (T = 0) was made approximately 1-2 minutes after addition of the substrate solution, employing excitation at 485 nm and emission at 530 nm, to determine the background fluorescence of the control sample. After the 3 hour incubation, the samples were read for fluorescence as above (T = 3 hours).

Calculation:

The Relative Fluorescence Unit (RFU) values were used to calculate the sample readings as follows:

$$RFU_{(T=3h)} - \text{Control } RFU_{(T=0)} = \text{Net } RFU_{(T=3h)}$$

The level of caspase cascade activation was determined by the ratio of the net RFU value for the test compound to that of the control samples. The EC_{50} (nM) was determined by a sigmoidal dose-response calculation (Prism 2.0,

GraphPad Software, Inc.). The compounds of the invention were determined to have caspase cascade activating effects by proceeding as in Example 8.

Table I. Caspase Potency

	EC_{50} (nM)	
Compound #	**T-47D**	**ZR-75-1**
70	345	163
72	3050	1950
74	3270	2080
79	557	349
85	6930	4207

EXAMPLE 9

Identification of Antineoplastic Activity in Cell Proliferation

T-47D and ZR-75-1 cells are grown and harvested by proceeding as in Example 8. An aliquot of 90 µL of cells (2.2 x 10^4 cells/mL) is added to a well of a 96-well microtiter plate containing 10 µL of a 10% DMSO in PRMI-1640 media solution containing 1 nM to 100 µM of test compound. An aliquot of 90 µL of cells is added to a well of a 96-well microtiter plate containing 10 µL of a 10% DMSO in RPMI-1640 media solution without test compound as the control sample for maximal cell proliferation (A_{max}). The samples are mixed by agitation and then incubated at 37°C for 48 hours in a 5% CO_2-95% humidity incubator. After incubation, the samples are removed from the incubator and 20 µL of CellTiter 96 Aqueous One Solution Cell Proliferation™ reagent (Promega) is added. The samples are mixed by agitation and incubated at 37°C for 2-4 hours in a 5% CO_2-95% humidity incubator. Using an absorbance plate reader (Model 1420 Wallac Instruments), an initial reading (T=0) is made approximately 1-2 minutes after addition of the solution, employing absorbance at 490 nm, to

determine any background absorbance of the test compound. After the 2-4 hours incubation, the samples are read for absorbance as above (A_{test}).

Baseline for the dose producing 50% inhibition of cell proliferation (GI_{50}) of initial cell numbers is determined by adding an aliquot of 90 µL of cells or 90 µL of media, respectively, to wells of a 96-well microtiter plate containing 10 µL of a 10% DMSO in RPMI-1640 media solution. The samples are mixed by agitation and then incubated at 37°C for 0.5 hours in a 5% CO_2-95% humidity incubator. After incubation, the samples are removed from the incubator and 20 µL of CellTiter 96 Aqueous One Solution Cell Proliferation™ reagent (Promega) is added. The samples are mixed by agitation and incubated at 37°C for 2-4 hours in a 5% CO_2-95% humidity incubator. Absorbance is read as above, ($A_{T=0}$) defining absorbance for initial cell number used as baseline GI_{50} determinations.

Calculation:

GI50 (nM) = 100 x [A_{test} - $A_{T=0)}$ / (A_{max} - $A_{T=0}$)].

EXAMPLE 10

Nuclear Fragmentation in T47D Cells

T47D cells are grown and harvested by proceeding as in Example 8 and treated with test compound followed by staining of the cell nuclei with Syto16, a fluorescent DNA dye which stains nuclei. Shrunken and fragmented nuclei are hallmarks of caspase-mediated apoptosis. T47D cells treated with test compound for 48 hours exhibit shrunken and fragmented nuclei.

EXAMPLE 11

Mitotic Arrest in Jurkat Cells

Jurkat cells are incubated with a range of concentrations of test compounds (0.02 µM to 5 µM) for 6 hours under normal growth conditions. Control cultures are treated with DMSO vehicle. The cells are then treated for

20 minutes with 800 nM Syto 16. Cytospin preparation are then prepared and the samples were viewed by fluorescent microscopy using a fluorescein filter set. For each concentration of test compound, the number of mitotic figures are counted and expressed as a percentage of the total number of cells. Three fields from each condition are evaluated and the mean and SEM were calculated and plotted as a function of drug concentration.

EXAMPLE 12

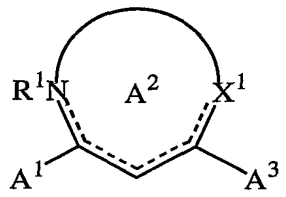
Cell Cycle Arrest in Solid Tumor Cell Lines

T47D cells are grown and harvested by proceeding as in Example 8. Cells at 1 x 10^6 are treated with test compound for 48 hours at 37°C. As a control, cells are also incubated with DMSO. Cells were harvested at 1200 rpm and washed twice with 5 mM EDTA/PBS. Cells are then resuspended in 300 µL of EDTA/PBS and 700 mL of 100% ethanol, vortexed and incubated at room temperature for 1 hour. Samples are spun down at 12000 rpm for 5 minutes and the supernatant is removed. A solution containing 100 µg/mL of propidium iodide and 1 mg/mL of RNAse A (fresh) is added to the samples and the samples are incubated for 1 hour at room temperature. Samples are then transferred to 12x75 mm polystyrene tubes and analyzed on a flow cytometer. All flow cytometry analyses are performed on FACScalibur (Becton Dickison) using Cell Quest analysis software.

Having now fully described this invention, it will be understood by those of ordinary skill in the art that the same can be performed within a wide and equivalent range of conditions, formulations and other parameters without affecting the scope of the invention or any embodiment thereof. All patents, patent applications and publications cited herein are fully incorporated by reference herein in their entirety.

What Is Claimed Is:

1. A compound of Formula I:



I

in which:

the dashed lines indicate optional unsaturation without violating valency rules;

R^1 is hydrogen, (C_{1-6})alkyl or $-C(O)R^6$, wherein R^6 is as defined below, or R^1 is absent when a double bond exists between the nitrogen atom to which R^1 is attached and an adjacent ring atom or R^1 is as defined below;

X^1 is $-NR^2-$, $-S-$, $-S(O)-$, $-S(O)_2-$ or $-O-$, wherein R^2 is hydrogen or (C_{1-6})alkyl or is absent when a double bond exists between the nitrogen atom to which R^2 is attached and an adjacent ring atom;

A^1 is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, or A^1 together with R^1 and the atoms to which A^1 and R^1 are attached forms a fused polycyclic ring system selected from heteroaryl and unsaturated, partially unsaturated or saturated heterocycloalkyl in any case containing a total of 10 to 15 ring atoms, wherein A^1 may be substituted with a group selected from $-X^2R^3$, $-X^2OR^3$, $-X^2C(O)R^3$, $-X^2OC(O)R^3$, $-X^2C(O)OR^3$, $-X^2SR^3$, $-X^2S(O)R^3$, $-X^2S(O)_2R^3$, $-X^2NR^3R^4$, $-X^2NR^4C(O)R^3$, $-X^2NR^4C(O)OR^3$, $-X^2C(O)NR^3R^4$, $-X^2NR^4C(O)NR^3R^4$, $-X^2NR^4C(NR^4)NR^3R^4$, $-X^2NR^4S(O)_2R^3$ and $-X^2S(O)_2NR^3R^4$, wherein X^2 is a bond or (C_{1-6})alkylene, R^3 is $-X^2R^5$ wherein X^2 is as defined above and R^5 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10

ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, wherein each ring within A^1 and R^5 contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A^1 and R^5 may be substituted further with 1 to 2 groups independently selected from (C_{1-6})alkylidene, oxo, imino and thioxo, with the proviso that only one of A^1 and R^5 is a fused polycyclic ring system;

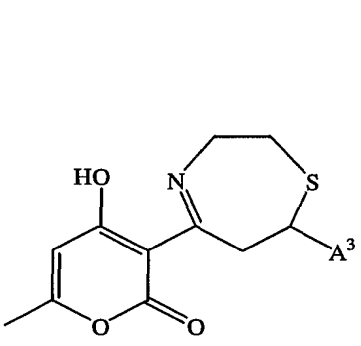
A^2 is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A^2 may be substituted with a group selected from $-X^2R^8$, $-X^2OR^8$, $-X^2C(O)R^8$, $-X^2OC(O)R^8$, $-X^2C(O)OR^8$, $-X^2SR^8$, $-X^2S(O)R^8$, $-X^2S(O)_2R^8$, $-X^2NR^4R^8$, $-X^2NR^4C(O)R^8$, $-X^2NR^4C(O)OR^8$, $-X^2C(O)NR^4R^8$, $-X^2NR^4C(O)NR^4R^8$, $-X^2NR^4C(NR^4)NR^4R^8$, $-X^2NR^4S(O)_2R^8$ and $-X^2S(O)_2NR^4R^8$, wherein X^2 is a bond or (C_{1-6})alkylene, R^8 is $-X^2R^9$ wherein X^2 is as defined above and R^9 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, wherein each ring within A^2 and R^8 contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$,

$-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A^2 and R^8 may be substituted further with 1 to 2 groups independently selected from (C_{1-6})alkylidene, oxo, imino and thioxo, with the proviso that only one of A^2 and R^8 is a fused polycyclic ring system; and

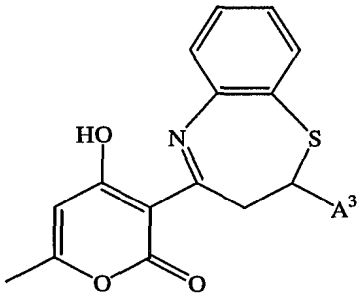
A^3 is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A^3 may be substituted with a group selected from $-X^2R^9$, $-X^2OR^9$, $-X^2C(O)R^9$, $-X^2OC(O)R^9$, $-X^2C(O)OR^9$, $-X^2SR^9$, $-X^2S(O)R^9$, $-X^2S(O)_2R^9$, $-X^2NR^4R^9$, $-X^2NR^4C(O)R^9$, $-X^2NR^4C(O)OR^9$, $-X^2C(O)NR^4R^9$, $-X^2NR^4C(O)NR^4R^9$, $-X^2NR^4C(NR^4)NR^4R^9$, $-X^2NR^4S(O)_2R^9$ and $-X^2S(O)_2NR^4R^9$, wherein X^2 is a bond or (C_{1-6})alkylene, R^9 is $-X^2R^{10}$ wherein X^2 is as defined above and R^{10} is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, wherein each ring within A^3 and R^{10} contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A^3 and R^{10} may be substituted further with 1 to 2 groups independently selected from (C_{1-6})alkylidene, oxo, imino and thioxo, with the proviso that only one of A^3 and R^{10} is a fused

polycyclic ring system; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof;

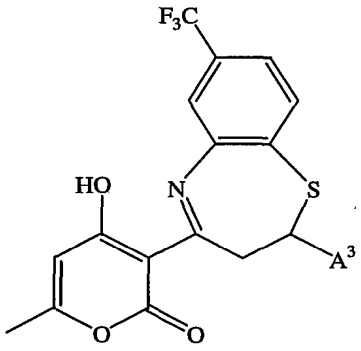
with the proviso that when said compound is selected from the group consisting of Formulae II(a), II(b) and II(c):



II(a)



II(b)



II(c)

then A^3 is other than:

unsubstituted pyridyl;

unsubstituted thienyl;

unsubstituted indolyl;

unsubstituted phenyl;

benzo[1,3]dioxolyl;

2,3-dihydro-benzo[1,4]dioxinyl;

phenyl which is mono-substituted by fluoro, bromo, iodo, nitro, methyl, isopropyl, ethoxy or methylsulfanyl; and

phenyl which is substituted by at least one of chloro, hydroxy or methoxy.

2. The compound of claim 1, and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts of said compound, with the further proviso that A^3 is other than:

unsubstituted pyridyl;

unsubstituted thienyl;

unsubstituted indolyl;

unsubstituted phenyl;

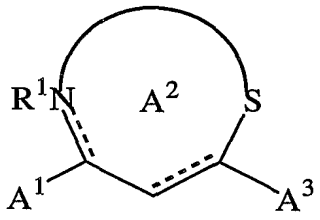
benzo[1,3]dioxolyl;

2,3-dihydro-benzo[1,4]dioxinyl; and

phenyl which is substituted by at least one of halogen, nitro, hydroxy, (C_{1-3})alkyl, methoxy, ethoxy and methylsulfanyl.

3. The compound of claim 1, and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts of said compound, with the further proviso that A^1 is not 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl.

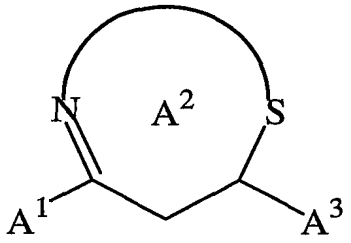
4. The compound of Claim 1 in which said compound is of Formula I(A):



I(A)

in which R^1, A^1, A^2 and A^3 are as defined in Claim 1; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

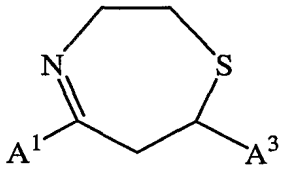
5. The compound of Claim 4 in which said compound is of Formula I(B):



I(B)

in which R^1, A^1, A^2 and A^3 are defined as in Claim 1; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

6. The compound of Claim 5 in which said A^2 is 2,3,6,7-tetrahydro-[1,4]thiazepin-5,7-ylene, that is the compound of Formula I(C):



I(C)

in which A^1 and A^3 are defined as in Claim 1, and said 2,3,6,7-tetrahydro-[1,4]thiazepin-5,7-ylene may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 is a bond or (C_{1-6})alkylene, R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

7. The compound of Claim 6 in which A^1 is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

8. The compound of Claim 7 in which said compound is selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-ethyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3[7-(2-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(3-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(4-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-[3-(3-trifluoromethyl-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-[3-(3,4-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-[3-(3,5-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(3-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-{7-[5-(2-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(3-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(4-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(2-chloro-5-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-[7-(4-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzenesulfonyl-1*H*-pyrrol-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(3-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(1-methyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3-chloro-2-methyl-5-trifluoromethyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(2,4-difluoro-benzenesulfonyl)-1*H*-pyrrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-(7-[2,2']bithienyl-5-yl-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(3,5-dichloro-phenyl)-1*H*-pyrrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(4-chloro-phenyl)-1*H*-pyrrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-chloro-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(6-*p*-tolylsulfanyl-imidazo[2,1-*b*]thiazol-5-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4,5-dibromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methylsulfanyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-chloro-1-methyl-3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(4-trifluoromethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-3-[7-(4-methanesulfonyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; and

3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-methoxy-6-methyl-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

9. The compound of Claim 6 in which A^1 is 4-hydroxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

10. The compound of Claim 9 in which said compound is selected from the group consisting of:

3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one; and

3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

11. The compound of Claim 6 in which A^1 is 2-hydroxy-6-oxo-cyclohex-1-enyl or 2-methoxy-6-oxo-cyclohex-1-enyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

12. The compound of Claim 11 in which said compound is selected from the group consisting of:

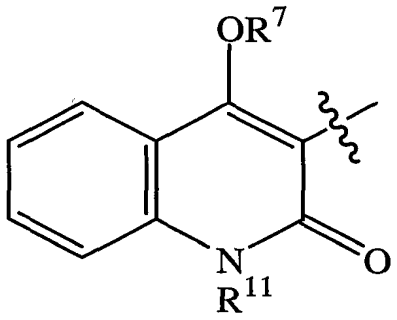
2-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

2-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone; and

3-hydroxy-2-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-cyclohex-2-enone;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

13. The compound of claim 6 in which A^1 is a group of Formula (c):



(c)

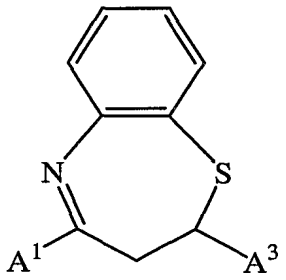
in which R^7 is hydrogen or methyl, R^{11} is hydrogen or (C_{1-6})alkyl and the free valence is attached to A^2; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

14. The compound of Claim 13 which is:

3-[7-2,4-dimethoxy-phenyl)-2,3,6,,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-1*H*-quinolin-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

15. The compound of Claim 5 in which said A^2 is 2,3-dihydro-benzo[*b*][1,4]thiazepin-5,7-ylene that is the compound-of Formula I(D):



I(D)

in which A^1 and A^3 are defined as in Claim 1, and said 2,3-dihydro-benzo[*b*][1,4]thiazepin-5,7-ylene may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 is a bond or (C_{1-6})alkylene, R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

16. The compound of Claim 15 in which A^1 is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

17. The compound of Claim 16 which is:

3-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-4-hydroxy-6-methyl-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

18. The compound of Claim 15 in which A^1 is 4-hydroxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

19. The compound of Claim 18 which is:

4-hydroxy-6-methyl-3-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-5,6-dihydro-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

20. The compound of Claim 15 in which A^1 is 2-hydroxy-6-oxo-cyclohex-1-enyl or 2-methoxy-6-oxo-cyclohex-1-enyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

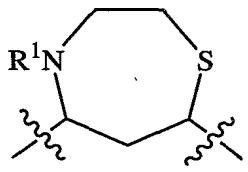
21. The compound of Claim 20 in which said compound is selected from the group consisting of:

3-hydroxy-2-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone; and

3-hydroxy-2-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

22. The compound of Claim 4 in which said A^2 is a group of Formula (k):



(k)

in which R^1 is defined as in Claim 1 and said group of Formula (k) may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$,

$-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 is a bond or (C_{1-6})alkylene, R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

23. The compound of Claim 22 in which R^1 is hydrogen; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

24. The compound of Claim 22 in which A^1 is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

25. The compound of Claim 24 in which said compound is selected from the group consisting of:

3-[4-acetyl-7-(2,4-dimethoxy-phenyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one; and

3-[7-(2,4-dimethoxy-phenyl)-4-(2,2,2-trifluoro-ethanoyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

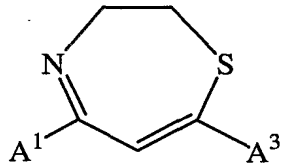
26. The compound of Claim 22 in which A^1 is optionally substituted phenyl.

27. The compound of Claim 26 which is:

1-[7-(2,4-dimethoxy-phenyl)-5-(3-fluoro-4-methoxyphenyl)-[1,4]thiazepan-4-yl]-ethanone;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

28. The compound of Claim 4 in which said A^2 is 2,3-dihydro-[1,4]thiazepin-5,7-ylene that is the compound of Formula I(F):



I(F)

in which A^1 and A^3 are defined as in Claim 1, and said 2,3-dihydro-[1,4]thiazepin-5,7-ylene may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 is a bond or (C_{1-6})alkylene, R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

29. The compound of Claim 28 in which A^1 is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

30. The compound of Claim 29 in which said compound is selected from the group consisting of:

3-[7-(2,4-dimethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; and

3-(7-[2,2′]bithienyl-5-yl-2,3-dihydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

31. The compound of Claim 28 in which A^1 is 4-hydroxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

32. The compound of Claim 31 which is:

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

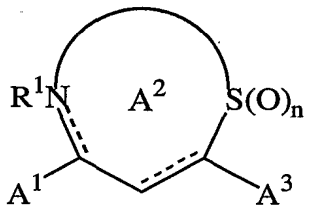
33. The compound of Claim 28 in which A^1 is 2-hydroxy-6-oxo-cyclohex-1-enyl or 2-methoxy-6-oxo-cyclohex-1-enyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

34. The compound of Claim 33 which is:

2-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

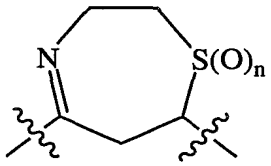
35. The compound of Claim 1 in which said compound is of Formula I(G):



I(G)

in which n, R^1, A^1, A^2 and A^3 are defined as in Claim 1; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

36. The compound of Claim 35 in which A^2 is a group of Formula (l):



(l)

in which n, and R^1 are defined as in Claim 1 and said group of Formula (l) may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 is a

bond or (C_{1-6})alkylene, R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

37. The compound of Claim 36 in which n is 1 and A^1 is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

38. The compound of Claim 37 which is:

3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1*H*-1λ^4-[1,4]thiazepin-5-yl]-4-hydroxy-6-methoxy-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

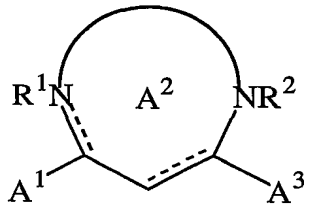
39. The compound of claim 36 in which n is 2 and A^1 is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

40. The compound of claim 39 which is:

3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3,6,7-tetrahydro-1*H*-1λ^6-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

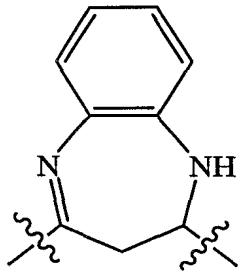
41. The compound of Claim 1 in which said compound is of Formula I(I):



I(I)

in which R^1, R^2, A^1, A^2 and A^3 are as defined in Claim 1; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

42. The compound of Claim 41 in which said A^2 is a group of Formula (j):



(j)

in which said group of Formula (j) may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 is a bond or (C_{1-6})alkylene, R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

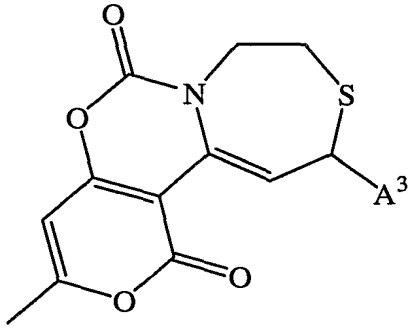
43. The compound of Claim 42 in which A^1 is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

44. The compound of Claim 43 which is:

3-[4-(2,4-dimethoxy-phenyl)-4,5-dihydro-3*H*-benzo[*b*][1,4]diazepin-2-yl]-4-hydroxy-6-methylpyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

45. The compound of Claim 1 in which said compound is of Formula I(K):



I(K)

in which A^3 is defined as in Claim 1; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

46. The compound of claim 45 which is:

10-(2,4-dimethoxy-phenyl)-3-methyl-7,8-dihydro-10*H*-2,5-dioxa-9-thia-6a-aza-cyclohepta[*a*]naphthalene-1,6-dione;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

47. A compound selected from the group consisting of:

4-hydroxy-3-[7-(2-methoxy-4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

3-[7-(2-chloro-5-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-3-[7-(4-chloro-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; and

4-hydroxy-3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer and mixtures of stereoisomers; or the pharmaceutically acceptable salt thereof.

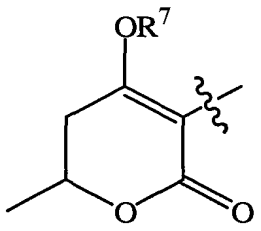
48. A compound selected from the group consisting of:

7-(2,4-dimethoxy-phenyl)-5-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2,2-dimethyl-2,3,6,7-tetrahydro-[1,4]thiazepine-3-carboxylic acid; and

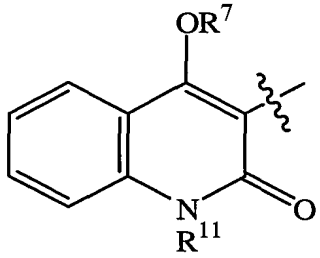
2-({1-[7-(2,4-dimethoxy-phenyl)-5-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2,2-dimethyl-2,3,6,7-tetrahydro-[1,4]thiazepin-3-yl]-methanoyl}-amino)-propionic acid *tert*-butyl ester;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof..

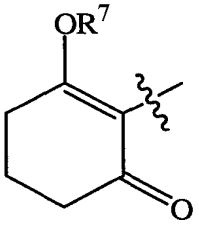
49. The compound of Claim 1 in which A^1 is a group selected from Formulae (b), (c), (d), (e) and (f):



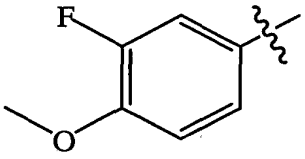
(b)



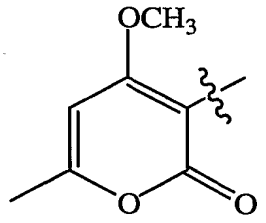
(c)



(d)



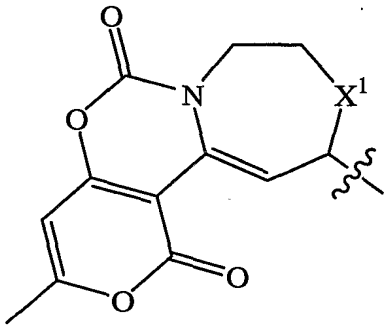
(e)



(f)

in which R^7 is hydrogen or methyl, R^{11} is hydrogen or (C_{1-6})alkyl and the free valance is attached to A^2, or

A^2 and A^1 together with R^1 and the atoms to which A^1 and R^1 are attached forms a group of Formula (g):



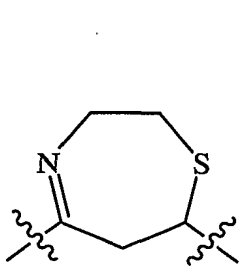
(g)

wherein X^1 is -S- and the free valance is attached to A^3; and

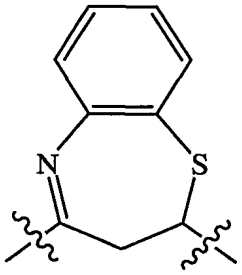
A^2 is as defined above or is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A^2 may be substituted with a group selected from $-X^2R^8$, $-X^2OR^8$, $-X^2C(O)R^8$, $-X^2OC(O)R^8$,

$-X^2C(O)OR^8$, $-X^2SR^8$, $-X^2S(O)R^8$, $-X^2S(O)_2R^8$, $-X^2NR^4R^8$, $-X^2NR^4C(O)R^8$, $-X^2NR^4C(O)OR^8$, $-X^2C(O)NR^4R^8$, $-X^2NR^4C(O)NR^4R^8$, $-X^2NR^4C(NR^4)NR^4R^8$, $-X^2NR^4S(O)_2R^8$ and $-X^2S(O)_2NR^4R^8$, wherein X^2 is a bond or (C_{1-6})alkylene, R^8 is $-X^2R^9$ wherein X^2 is as defined above and R^9 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, wherein each ring within A^2 and R^8 contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and wherein any said heteroalkylene, carbocycloalkyl and heterocycloalkyl rings within A^2 and R^8 may be substituted further with 1 to 2 groups independently selected from (C_{1-6})alkylidene, oxo, imino and thioxo, with the proviso that only one of A^2 and R^8 is a fused polycyclic ring system; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

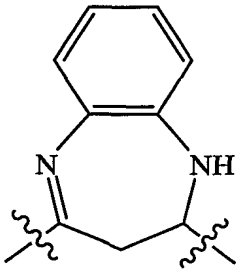
50. The compound of Claim 49 in which A^2 is a group selected from Formulae (h), (i), (j), (k), (l) and (m):



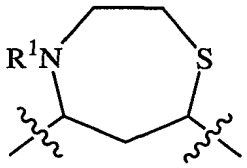
(h)



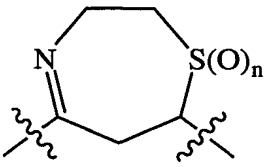
(i)



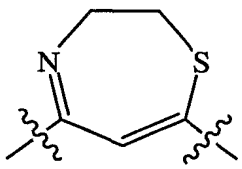
(j)



(k)

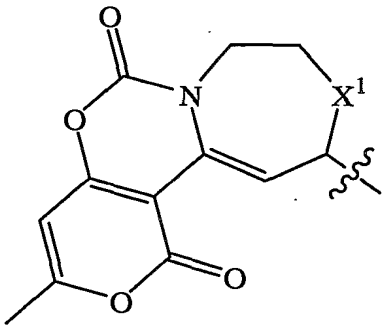


(l)



(m)

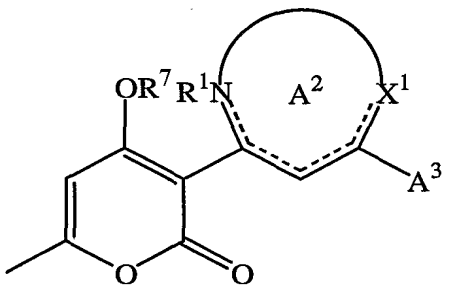
in which n is 1 or 2 and R^1 is acetyl or trifluoroacetyl or A^2 and A^1 together with R^1 and the atoms to which A^1 and R^1 are attached forms a group of Formula (g):



(g)

wherein X^1 is -S- and the free valance is attached to A^3; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

51. A compound of Formula II:



II

in which:

the dashed lines indicate optional unsaturation without violating valency rules;

R^1 is hydrogen, (C_{1-6})alkyl or $-C(O)R^6$, wherein R^6 is as defined below, or R^1 is absent when a double bond exists between the nitrogen atom to which R^1 is attached and an adjacent ring atom or R^1 is as defined below;

R^7 is hydrogen;

X^1 is $-NR^2-$, $-S-$, $-S(O)-$, $-S(O)_2-$ or $-O-$, wherein R^2 is hydrogen or (C_{1-6})alkyl or is absent when a double bond exists between the nitrogen atom to which R^2 is attached and an adjacent ring atom;

A^2 is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A^2 may be substituted with a group selected from $-R^8$, $-X^2OR^8$, $-X^2C(O)R^8$, $-X^2OC(O)R^8$, $-X^2C(O)OR^8$, $-X^2SR^8$, $-X^2S(O)R^8$, $-X^2S(O)_2R^8$, $-X^2NR^4R^8$, $-X^2NR^4C(O)R^8$, $-X^2NR^4C(O)OR^8$, $-X^2C(O)NR^4R^8$, $-X^2NR^4C(O)NR^4R^8$, $-X^2NR^4C(NR^4)NR^4R^8$, $-X^2NR^4S(O)_2R^8$ and $-X^2S(O)_2NR^4R^8$, wherein X^2 is a bond or (C_{1-6})alkylene, R^8 is $-X^2R^9$ wherein X^2 is as defined above and R^9 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, wherein each ring within A^2 and R^8 contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$,

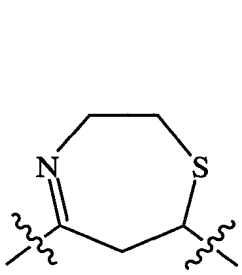
$-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$,$-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and wherein any said heteroalkylene, carbocycloalkyl and heterocycloalkyl rings within A^2 and R^8 may be substituted further with 1 to 2 groups independently selected from (C_{1-6})alkylidene, oxo, imino and thioxo with the proviso that only one of A^2 and R^8 is a fused polycyclic ring system; and

A^3 is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A^3 may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2C(O)R^9$, $-X^2OC(O)R^9$, $-X^2C(O)OR^9$, $-X^2SR^9$, $-X^2S(O)R^9$, $-X^2S(O)_2R^9$, $-X^2NR^4R^9$, $-X^2NR^4C(O)R^9$, $-X^2NR^4C(O)OR^9$, $-X^2C(O)NR^4R^9$, $-X^2NR^4C(O)NR^4R^9$, $-X^2NR^4C(NR^4)NR^4R^9$, $-X^2NR^4S(O)_2R^9$ and $-X^2S(O)_2NR^4R^9$, wherein X^2 is a bond or (C_{1-6})alkylene, R^9 is $-X^2R^{10}$ wherein X^2 is as defined above and R^{10} is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, wherein each ring within A^3 and R^{10} contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$,$-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A^3 and R^{10} may be substituted further with 1 to 2 groups independently selected from (C_{1-6})alkylidene, oxo, imino and thioxo with

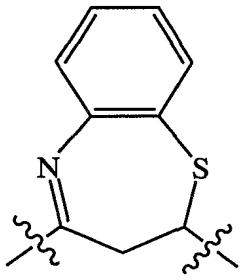
the proviso that only one of A^3 and R^{10} is a fused polycyclic ring system; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof;

provided, however, Formula II does not represent a compound wherein A^2 is 2,3,6,7-tetrahydro-[1,4]thiazepinylene, 2,3-dihydro-benzo[*b*][1,4]thiazepinylene or 7-trifluoro-2,3-dihydro-benzo[*b*][1,4]thiazepinylene and A^3 is benzo[1,3]dioxolyl, indolyl, phenyl, pyridyl or thienyl, wherein said phenyl may be substituted with 1 to 3 groups independently selected from halo, nitro, hydroxy, (C_{1-4})alkyl, (C_{1-4})alkylsulfanyl and (C_{1-4})alkyloxy or any *N*-oxide derivative; protected derivative, individual stereoisomer or mixture of stereoisomers, or pharmaceutically acceptable salt thereof.

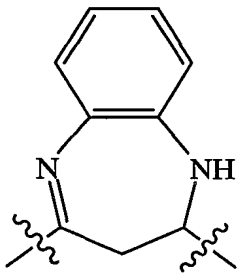
52. The compound of Claim 51 in which A^2 is a group selected from Formulae (h), (i), (j), (k), (l) and (m):



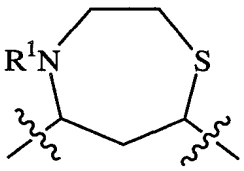
(h)



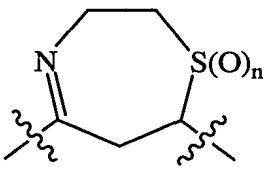
(i)



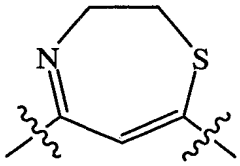
(j)



(k)

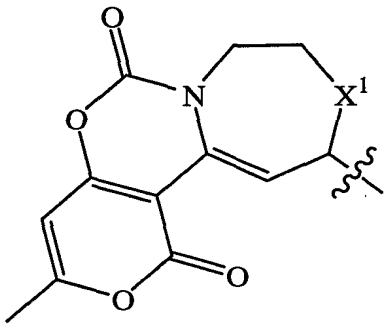


(l)



(m)

in which n is 1 or 2 and R^1 is acetyl or trifluoroacetyl or A^2 and A^1 together with R^1 and the atoms to which A^1 and R^1 are attached forms a group of Formula (g):



(g)

wherein X^1 is -S- and the free valance is attached to A^3; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

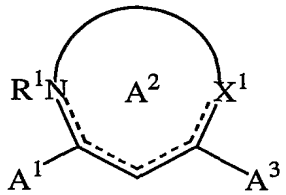
53. The compound of Claim 52 in which A^3 is phenyl or heteroaryl containing a total of 5 to 9 ring atoms, wherein A^3 may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2SR^9$ and $-X^2S(O)_2R^9$, wherein R^9 is $-X^2R^{10}$, X^2 is a bond or (C_{1-6})alkylene and R^{10} is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within A^3 and R^{10} may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, halo, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2SR^4$, $-X^2S(O)_2R^6$ and $-X^2NR^4R^4$, wherein R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

54. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1, 47 or 51 or a *N*-oxide derivative, prodrug derivative, individual isomer or mixture of isomers or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable excipient.

55. The pharmaceutical composition of Claim 54, further comprising at least one known cancer chemotherapeutic agent.

56. The pharmaceutical composition of Claim 55, wherein said cancer therapeutic agent is selected from the group consisting of busulfan, cis-platin, mitomycin C, carboplatin, colchicine, vinblastine, paclitaxel, docetaxel, camptothecin, topotecan, doxorubicin, etoposide, 5-azacytidine, 5-fluorouracil, methotrexate, 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea, thioguanine, melphalan, chlorambucil, cyclophosamide, ifosfamide, vincristine, mitoguazone, epirubicin, aclarubicin, bleomycin, imitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen, Herceptin®, Rituxan® and alanosine.

57. A method of treating a disorder responsive to the induction of apoptosis in an animal suffering said disorder, comprising administering to a mammal in need of such treatment an effective amount of a compound of Formula I:



I

in which:

the dashed lines indicate optional unsaturation without violating valency rules;

R^1 is hydrogen, (C_{1-6})alkyl or $-C(O)R^6$, wherein R^6 is as defined below, or R^1 is absent when a double bond exists between the nitrogen atom to which R^1 is attached and an adjacent ring atom or R^1 is as defined below;

X^1 is $-NR^2-$, -S-, -S(O)-, $-S(O)_2-$ or -O-, wherein R^2 is hydrogen or (C_{1-6})alkyl or is absent when a double bond exists between the nitrogen atom to which R^2 is attached and an adjacent ring atom;

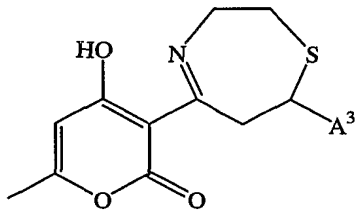
A^1 is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, or A^1 together with R^1 and the atoms to which A^1 and R^1 are attached forms a fused polycyclic ring system selected from heteroaryl and unsaturated, partially unsaturated or saturated heterocycloalkyl in any case containing a total of 10 to 15 ring atoms, wherein A^1 may be substituted with a group selected from $-R^3$, $-X^2OR^3$, $-X^2C(O)R^3$, $-X^2OC(O)R^3$, $-X^2C(O)OR^3$, $-X^2SR^3$, $-X^2S(O)R^3$, $-X^2S(O)_2R^3$, $-X^2NR^3R^4$, $-X^2NR^4C(O)R^3$, $-X^2NR^4C(O)OR^3$, $-X^2C(O)NR^3R^4$, $-X^2NR^4C(O)NR^3R^4$, $-X^2NR^4C(NR^4)NR^3R^4$, $-X^2NR^4S(O)_2R^3$ and $-X^2S(O)_2NR^3R^4$, wherein X^2 is a bond or (C_{1-6})alkylene, R^3 is $-X^2R^5$ wherein X^2 is as defined above and R^5 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, wherein each ring within A^1 and R^5 contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A^1 and R^5 may be substituted further with 1 to 2 groups independently selected from (C_{1-6})alkylidene, oxo, imino and thioxo, with the provisos that only one of A^1 and R^5 is a fused polycyclic ring system;

A^2 is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A^2 may be substituted with a group selected

from -R^8, -X^2OR^8, -$X^2C(O)R^8$, -$X^2OC(O)R^8$, -$X^2C(O)OR^8$, -X^2SR^8, -$X^2S(O)R^8$, -$X^2S(O)_2R^8$, -$X^2NR^4R^8$, -$X^2NR^4C(O)R^8$, -$X^2NR^4C(O)OR^8$, -$X^2C(O)NR^4R^8$, -$X^2NR^4C(O)NR^4R^8$, -$X^2NR^4C(NR^4)NR^4R^8$, -$X^2NR^4S(O)_2R^8$ and -$X^2S(O)_2NR^4R^8$, wherein X^2 is a bond or (C_{1-6})alkylene, R^8 is -X^2R^9 wherein X^2 is as defined above and R^9 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, wherein each ring within A^2 and R^8 contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, -X^2OR^4, -$X^2C(O)R^6$, -$X^2OC(O)R^6$, -$X^2C(O)OR^4$, -X^2SR^4, -$X^2S(O)R^6$, -$X^2S(O)_2R^6$, -$X^2NR^4R^4$, -$X^2NR^4C(O)R^6$, -$X^2NR^4C(O)OR^4$, -$X^2C(O)NR^4R^4$, -$X^2NR^4C(O)NR^4R^4$, -$X^2NR^4C(NR^4)NR^4R^4$, -$X^2C(O)NR^4X^2C(O)OR^4$, -$X^2NR^4S(O)_2R^6$ and -$X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A^2 and R^8 may be substituted further with 1 to 2 groups independently selected from (C_{1-6})alkylidene, oxo, imino and thioxo, with the proviso that only one of A^2 and R^8 is a fused polycyclic ring system; and

A^3 is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A^3 may be substituted with a group selected from -R^9, -X^2OR^9, -$X^2C(O)R^9$, -$X^2OC(O)R^9$, -$X^2C(O)OR^9$, -X^2SR^9, -$X^2S(O)R^9$, -$X^2S(O)_2R^9$, -$X^2NR^4R^9$, -$X^2NR^4C(O)R^9$, -$X^2NR^4C(O)OR^9$, -$X^2C(O)NR^4R^9$, -$X^2NR^4C(O)NR^4R^9$, -$X^2NR^4C(NR^4)NR^4R^9$, -$X^2NR^4S(O)_2R^9$ and -$X^2S(O)_2NR^4R^9$, wherein X^2 is a bond or (C_{1-6})alkylene, R^9 is -X^2R^{10} wherein X^2 is as defined above and R^{10} is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated,

partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, wherein each ring within A^3 and R^{10} contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A^3 and R^{10} may be substituted further with 1 to 2 groups independently selected from (C_{1-6})alkylidene, oxo, imino and thioxo, with the proviso that only one of A^3 and R^{10} is a fused polycyclic ring system; or an *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers, or a pharmaceutically acceptable salt thereof; with the proviso that when said compound is of Formula II(a):



II(a)

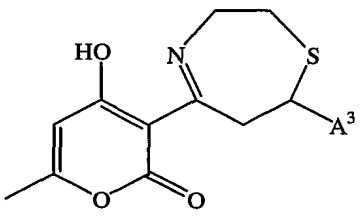
then A^3 is other than:

(a) benzo[1,3]dioxolyl;

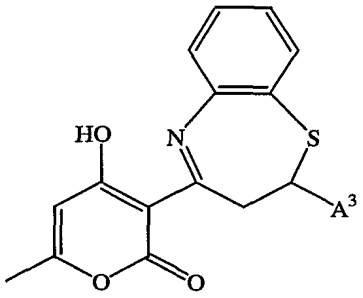
(b) phenyl which is mono-substituted by bromo, hydroxy, methyl or isopropyl; and

(c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino.

58. The method of claim 57, with the further proviso that when said compound is selected from the group consisting of Formula II(a) and II(b):



II(a)



II(b)

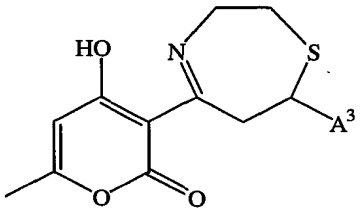
then A^3 is other than:

(a) benzo[1,3]dioxolyl;

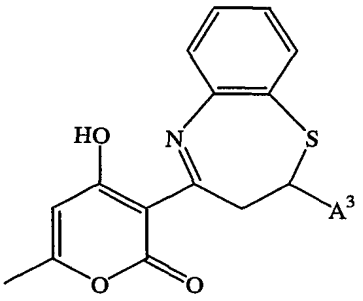
(b) phenyl which is mono-substituted by bromo, nitro, hydroxy, methyl, or isopropyl; and

(c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino.

59. The method of claim 57, with the further proviso that when said compound is selected from the group consisting of Formula II(a) and II(b):



II(a)



II(b)

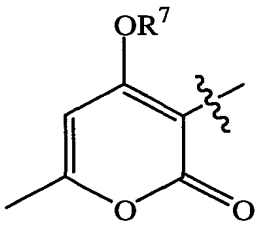
then A^3 is other than:

(a) benzo[1,3]dioxolyl;

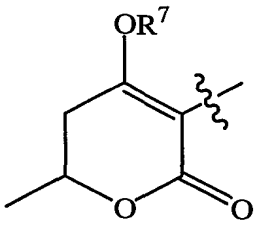
(b) 2,3-dihydro-benzo[1,4]dioxinyl; and

(c) phenyl which is substituted by at least one of bromo, chloro, hydroxy, nitro, methoxy and (C_{1-3})alkyl.

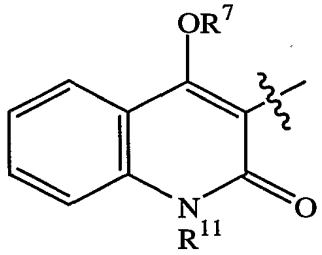
60. The method of Claim 57, wherein A^1 of said compound is a group selected from Formulae (a), (b), (c), (d) and (e):



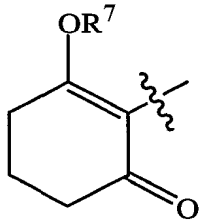
(a)



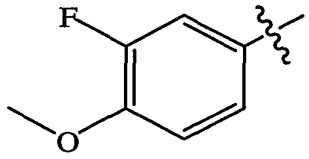
(b)



(c)



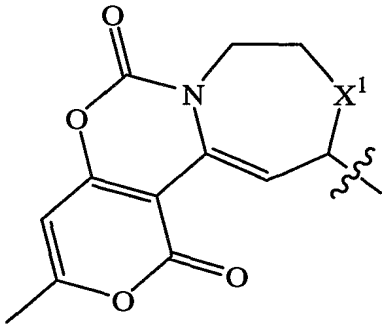
(d)



(e)

in which R^7 is hydrogen or methyl, R^{11} is hydrogen or (C_{1-6})alkyl and the free valance is attached to A^2, or

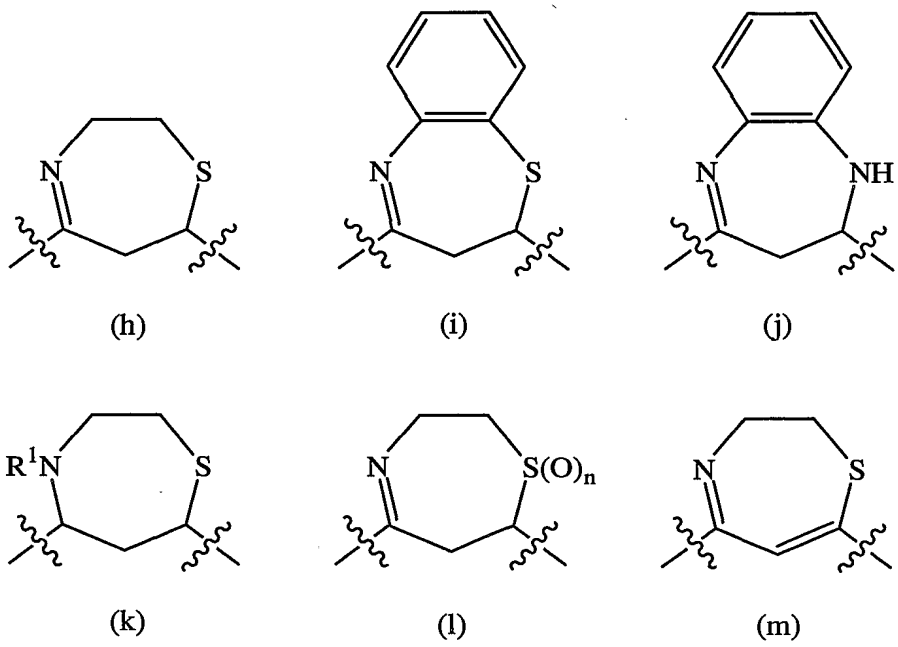
A^2 and A^1 together with R^1 and the atoms to which A^1 and R^1 are attached forms a group of Formula (g):



(g)

wherein X^1 is -S- and the free valance is attached to A^3; and

A^2 of said compound is as defined above or is a group selected from Formulae (h), (i), (j), (k), (l) and (m):



(h) (i) (j)

(k) (l) (m)

in which n is 1 or 2 and R^1 is acetyl or trifluoroacetyl; or an *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers, or a pharmaceutically acceptable salt thereof.

61. The method of Claim 60, wherein A^3 of said compound is phenyl or heteroaryl containing a total of 5 to 9 ring atoms, wherein A^3 may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2SR^9$ and $-X^2S(O)_2R^9$, wherein R^9 is $-X^2R^{10}$, X^2 is a bond or (C_{1-6})alkylene and R^{10} is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within A^3 and R^{10} may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, halo, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2SR^4$, $-X^2S(O)_2R^6$ and $-X^2NR^4R^4$, wherein R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

62. The method of Claim 61, wherein said compound is selected from the group consisting of:

2-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

4-hydroxy-3-[7-(4-methanesulfonyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

3-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

3-hydroxy-2-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-cyclohex-2-enone;

3-hydroxy-2-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone;

4-hydroxy-6-methyl-3-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-5,6-dihydro-pyran-2-one; and

4-hydroxy-6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-5,6-dihydro-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

63. The method of claim 57, wherein said compound is selected from the list consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[4-acetyl-7-(2,4-dimethoxy-phenyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-4-(2,2,2-trifluoro-ethanoyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

1-[7-(2,4-dimethoxy-phenyl)-5-(3-fluoro-4-methoxyphenyl)-[1,4]thizepan-4-yl]-ethanone;

4-hydroxy-6-methyl-3-[7-(3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-ethyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3[7-(2-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(3-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(4-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-[3-(3-trifluoromethyl-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-[3-(3,4-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-[3-(3,5-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(3-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-{7-[5-(2-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(3-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(4-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(2-chloro-5-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-[7-(4-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzenesulfonyl-1*H*-pyrrol-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(3-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(1-methyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3-chloro-2-methyl-5-trifluoromethyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(2,4-difluoro-benzenesulfonyl)-1*H*-pyrrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-(7-[2,2′]bithienyl-5-yl-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(3,5-dichloro-phenyl)-1*H*-pyrrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(4-chloro-phenyl)-1*H*-pyrrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-chloro-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(6-*p*-tolylsulfanyl-imidazo[2,1-*b*]thiazol-5-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4,5-dibromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2-chloro-5-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methylsulfanyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-chloro-1-methyl-3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[4-(2,4-dimethoxy-phenyl)-4,5-dihydro-3*H*-benzo[*b*][1,4]diazepin-2-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-2,4-dimethoxy-phenyl)-2,3,6,,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-1*H*-quinolin-2-one;

4-hydroxy-6-methyl-3-[7-(4-trifluoromethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-hydroxy-2-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone;

3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1*H*-1λ^4-[1,4]thiazepin-5-yl]-4-hydroxy-6-methoxy-pyran-2-one;

10-(2,4-dimethoxy-phenyl)-3-methyl-7,8-dihydro-10*H*-2,5-dioxa-9-thia-6a-aza-cyclohepta[*a*]naphthalene-1,6-dione;

3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3,6,7-tetrahydro-1*H*-1λ^6-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-(7-[2,2']bithienyl-5-yl-2,3-dihydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone; and

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

64. A method of treating a disorder responsive to the induction of apoptosis in an animal suffering said disorder, comprising administering to a mammal in need of such treatment an effective amount of a compound selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4-ethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(3-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

3-[7-(2-bromo-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,3-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]4-hydroxy-6-methyl-pyran-2-one;

3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

6-methyl-3-(2-*p*-tolyl-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl)-pyran-2-one;

4-hydroxy-6-methyl-3-[2-(4-methylsulfanyl-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-pyran-2-one; and

3-[7-(2,4-dimethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-3-[7-(4-chloro-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; and

4-hydroxy-3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

65. The method of claim 64, wherein said compound is selected from the group consisting of:

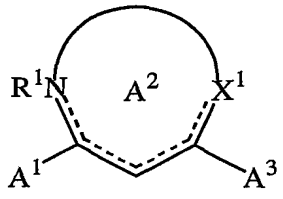
4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; and

6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

66. A method for treating or preventing cancer, comprising administering to an animal in need of such treatment an effective amount of a compound of Formula I:



I

in which:

the dashed lines indicate optional unsaturation without violating valency rules;

R^1 is hydrogen, (C_{1-6})alkyl or $-C(O)R^6$, wherein R^6 is as defined below, or R^1 is absent when a double bond exists between the nitrogen atom to which R^1 is attached and an adjacent ring atom or R^1 is as defined below;

X^1 is $-NR^2-$, $-S-$, $-S(O)-$, $-S(O)_2-$ or $-O-$, wherein R^2 is hydrogen or (C_{1-6})alkyl or is absent when a double bond exists between the nitrogen atom to which R^2 is attached and an adjacent ring atom;

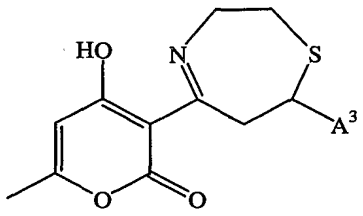
A^1 is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, or A^1 together with R^1 and the atoms to which A^1 and R^1 are attached forms a fused polycyclic ring system selected from heteroaryl and unsaturated, partially unsaturated or saturated heterocycloalkyl in any case containing a total of 10 to 15 ring atoms, wherein A^1 may be substituted with a group selected from $-R^3$, $-X^2OR^3$, $-X^2C(O)R^3$, $-X^2OC(O)R^3$, $-X^2C(O)OR^3$, $-X^2SR^3$, $-X^2S(O)R^3$, $-X^2S(O)_2R^3$, $-X^2NR^3R^4$, $-X^2NR^4C(O)R^3$, $-X^2NR^4C(O)OR^3$, $-X^2C(O)NR^3R^4$, $-X^2NR^4C(O)NR^3R^4$, $-X^2NR^4C(NR^4)NR^3R^4$, $-X^2NR^4S(O)_2R^3$ and $-X^2S(O)_2NR^3R^4$, wherein X^2 is a bond or (C_{1-6})alkylene, R^3 is $-X^2R^5$ wherein X^2 is as defined above and R^5 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, wherein each ring within A^1 and R^5 contains from 3 to 8 ring atoms and may be

substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A^1 and R^5 may be substituted further with 1 to 2 groups independently selected from (C_{1-6})alkylidene, oxo, imino and thioxo, with the provisos that only one of A^1 and R^5 is a fused polycyclic ring system;

A^2 is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A^2 may be substituted with a group selected from $-R^8$, $-X^2OR^8$, $-X^2C(O)R^8$, $-X^2OC(O)R^8$, $-X^2C(O)OR^8$, $-X^2SR^8$, $-X^2S(O)R^8$, $-X^2S(O)_2R^8$, $-X^2NR^4R^8$, $-X^2NR^4C(O)R^8$, $-X^2NR^4C(O)OR^8$, $-X^2C(O)NR^4R^8$, $-X^2NR^4C(O)NR^4R^8$, $-X^2NR^4C(NR^4)NR^4R^8$, $-X^2NR^4S(O)_2R^8$ and $-X^2S(O)_2NR^4R^8$, wherein X^2 is a bond or (C_{1-6})alkylene, R^8 is $-X^2R^9$ wherein X^2 is as defined above and R^9 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, wherein each ring within A^2 and R^8 contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A^2 and R^8 may be substituted further with 1 to 2 groups independently selected from

(C_{1-6})alkylidene, oxo, imino and thioxo, with the proviso that only one of A^2 and R^8 is a fused polycyclic ring system; and

A^3 is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A^3 may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2C(O)R^9$, $-X^2OC(O)R^9$, $-X^2C(O)OR^9$, $-X^2SR^9$, $-X^2S(O)R^9$, $-X^2S(O)_2R^9$, $-X^2NR^4R^9$, $-X^2NR^4C(O)R^9$, $-X^2NR^4C(O)OR^9$, $-X^2C(O)NR^4R^9$, $-X^2NR^4C(O)NR^4R^9$, $-X^2NR^4C(NR^4)NR^4R^9$, $-X^2NR^4S(O)_2R^9$ and $-X^2S(O)_2NR^4R^9$, wherein X^2 is a bond or (C_{1-6})alkylene, R^9 is $-X^2R^{10}$ wherein X^2 is as defined above and R^{10} is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, wherein each ring within A^3 and R^{10} contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A^3 and R^{10} may be substituted further with 1 to 2 groups independently selected from (C_{1-6})alkylidene, oxo, imino and thioxo, with the proviso that only one of A^3 and R^{10} is a fused polycyclic ring system; or an *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers, or a pharmaceutically acceptable salt thereof; with the proviso that when said compound is of Formula II(a):



II(a)

then A^3 is other than:

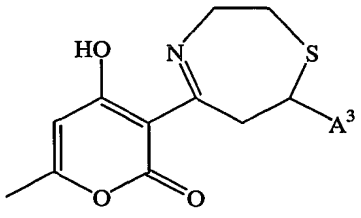
(a) benzo[1,3]dioxolyl;

(b) phenyl which is mono-substituted by bromo, hydroxy, methyl or isopropyl; and

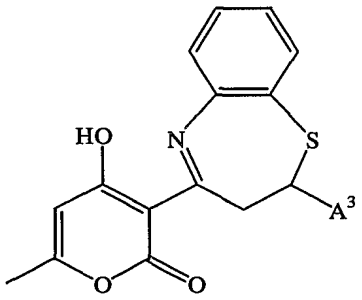
(c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

67. The method of claim 66, with the further proviso that when said compound is selected the group consisting of Formula II(a) and II(b):



II(a)



II(b)

then A^3 is other than:

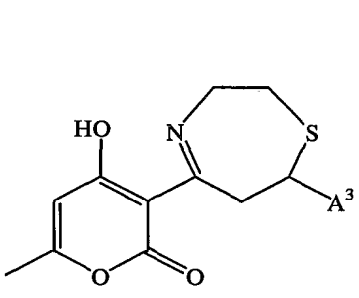
(a) benzo[1,3]dioxolyl;

(b) phenyl which is mono-substituted by bromo, nitro, hydroxy, methyl, or isopropyl; and

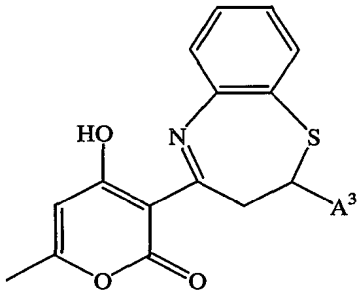
(c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

68. The method of claim 66, with the further proviso that when said compound is selected the group consisting of Formula II(a) and II(b):



II(a)



II(b)

then A^3 is other than:

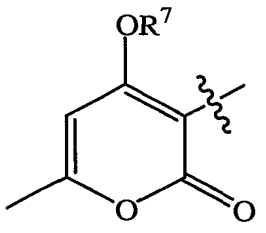
(a) benzo[1,3]dioxolyl;

(b) 2,3-dihydro-benzo[1,4]dioxinyl; and

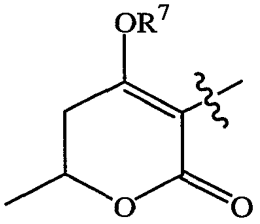
(c) phenyl which is substituted by at least one of bromo, chloro, hydroxy, nitro, methoxy and (C_{1-3})alkyl; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof..

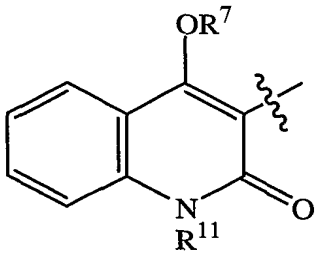
69. The method of Claim 66, wherein A^1 of said compound is a group selected from Formulae (a), (b), (c), (d) and (e):



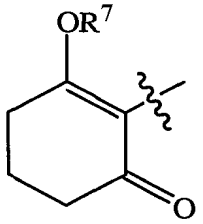
(a)



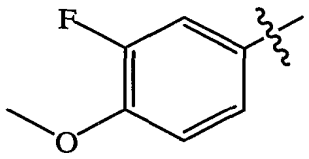
(b)



(c)



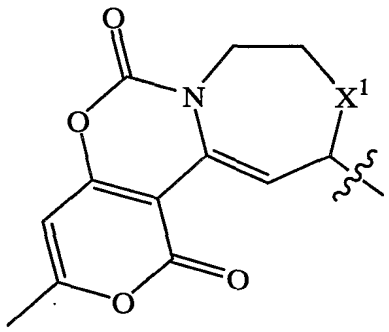
(d)



(e)

in which R^7 is hydrogen or methyl, R^{11} is hydrogen or (C_{1-6})alkyl and the free valance is attached to A^2, or

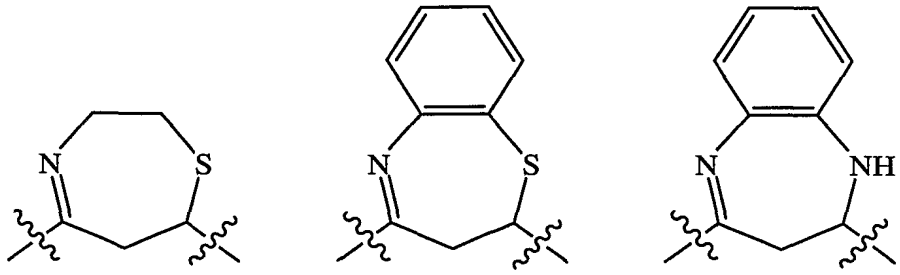
A^2 and A^1 together with R^1 and the atoms to which A^1 and R^1 are attached forms a group of Formula (g):



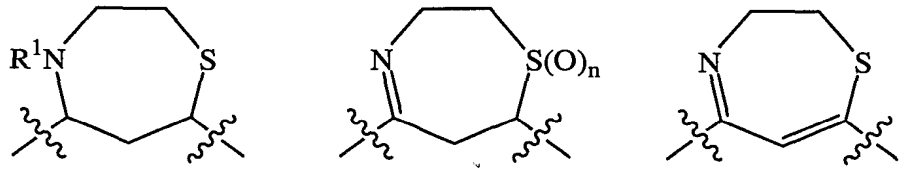
(g)

wherein X^1 is -S- and the free valance is attached to A^3; and

A^2 of said compound is as defined above or is a group selected from Formulae (h), (i), (j), (k), (l) and (m):



(h) (i) (j)



(k) (l) (m)

in which n is 1 or 2 and R^1 is acetyl or trifluoroacetyl; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

70. The method of Claim 69, wherein A^3 of said compound is phenyl or heteroaryl containing a total of 5 to 9 ring atoms, wherein A^3 may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2SR^9$ and $-X^2S(O)_2R^9$, wherein R^9 is $-X^2R^{10}$, X^2 is a bond or (C_{1-6})alkylene and R^{10} is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within A^3 and R^{10} may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, halo, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2SR^4$, $-X^2S(O)_2R^6$ and $-X^2NR^4R^4$, wherein R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

71. The method of Claim 70, wherein said compound is selected from the group consisting of:

4-hydroxy-3-[7-(2-methoxy-4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

2-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

4-hydroxy-3-[7-(4-methanesulfonyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

3-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

3-hydroxy-2-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-cyclohex-2-enone;

3-hydroxy-2-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone;

4-hydroxy-6-methyl-3-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-5,6-dihydro-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-5,6-dihydro-pyran-2-one; and

3-[7-(2,4-dimethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

72. The method of claim 66, wherein said compound is selected from the list consisting of:

3-[4-acetyl-7-(2,4-dimethoxy-phenyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-4-(2,2,2-trifluoro-ethanoyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

1-[7-(2,4-dimethoxy-phenyl)-5-(3-fluoro-4-methoxyphenyl)-[1,4]thizepan-4-yl]-ethanone;

4-hydroxy-6-methyl-3-[7-(3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-ethyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3[7-(2-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(3-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(4-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-[3-(3-trifluoromethyl-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-[3-(3,4-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-[3-(3,5-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(3-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-{7-[5-(2-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(3-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(4-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(2-chloro-5-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-[7-(4-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzenesulfonyl-1*H*-pyrrol-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(3-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(1-methyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3-chloro-2-methyl-5-trifluoromethyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(2,4-difluoro-benzenesulfonyl)-1*H*-pyrrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-(7-[2,2']bithienyl-5-yl-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(3,5-dichloro-phenyl)-1*H*-pyrrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(4-chloro-phenyl)-1*H*-pyrrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-chloro-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(6-*p*-tolylsulfanyl-imidazo[2,1-*b*]thiazol-5-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4,5-dibromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2-chloro-5-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methylsulfanyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-chloro-1-methyl-3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[4-(2,4-dimethoxy-phenyl)-4,5-dihydro-3*H*-benzo[*b*][1,4]diazepin-2-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-2,4-dimethoxy-phenyl)-2,3,6,,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-1*H*-quinolin-2-one;

4-hydroxy-6-methyl-3-[7-(4-trifluoromethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-hydroxy-2-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone;

3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1*H*-1λ^4-[1,4]thiazepin-5-yl]-4-hydroxy-6-methoxy-pyran-2-one;

10-(2,4-dimethoxy-phenyl)-3-methyl-7,8-dihydro-10*H*-2,5-dioxa-9-thia-6a-aza-cyclohepta[*a*]naphthalene-1,6-dione;

3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3,6,7-tetrahydro-1*H*-1λ^6-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-(7-[2,2′]bithienyl-5-yl-2,3-dihydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone; and

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

73. A method for treating or preventing cancer, comprising administering to an animal in need of such treatment an effective amount of a compound selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4-ethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(3-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

3-[7-(2-bromo-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,3-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]4-hydroxy-6-methyl-pyran-2-one;

3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

6-methyl-3-(2-*p*-tolyl-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl)-pyran-2-one;

4-hydroxy-6-methyl-3-[2-(4-methylsulfanyl-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-pyran-2-one;

4-hydroxy-3-[7-(4-chloro-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; and

4-hydroxy-3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

74. The method of claim 73, wherein said compound is selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; and

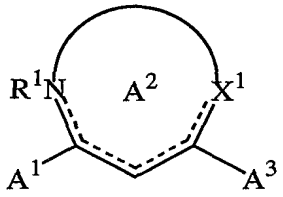
6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

75. The method of Claims 66 and 73, wherein said cancer is selected from the group consisting of Hodgkin's disease, non-Hodgkin's lymphoma, acute and chronic lymphocytic leukemias, multiple myeloma, neuroblastoma, breast carcinoma, ovarian carcinoma, lung carcinoma, Wilms' tumor, cervical carcinoma, testicular carcinoma, soft-tissue sarcoma, chronic lymphocytic leukemia, primary macroglobulinemia, bladder carcinoma, chronic granulocytic leukemia, primary brain carcinoma, malignant melanoma, small-cell lung carcinoma, stomach carcinoma, colon carcinoma, malignant pancreatic insulinoma, malignant carcinoid carcinoma, choriocarcinoma, mycosis fungoides,

head and neck carcinoma, osteogenic sarcoma, pancreatic carcinoma, acute granulocytic leukemia, hairy cell leukemia, neuroblastoma, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinoma, thyroid carcinoma, esophageal carcinoma, malignant hypercalcemia, cervical hyperplasia, renal cell carcinoma, endometrial carcinoma, polycythemia vera, essential thrombocytosis, adrenal cortex carcinoma, skin cancer an prostatic carcinoma.

76. A method for the treatment of drug resistant cancer, comprising administering to an animal in need of such treatment an effective amount of a compound of compound of Formula I:



I

in which:

the dashed lines indicate optional unsaturation without violating valency rules;

R^1 is hydrogen, (C_{1-6})alkyl or $-C(O)R^6$, wherein R^6 is as defined below, or R^1 is absent when a double bond exists between the nitrogen atom to which R^1 is attached and an adjacent ring atom or R^1 is as defined below;

X^1 is $-NR^2-$, -S-, -S(O)-, $-S(O)_2-$ or -O-, wherein R^2 is hydrogen or (C_{1-6})alkyl or is absent when a double bond exists between the nitrogen atom to which R^2 is attached and an adjacent ring atom;

A^1 is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, or A^1 together with R^1 and the atoms to which A^1 and R^1 are attached forms a fused polycyclic ring system selected from heteroaryl and unsaturated, partially unsaturated or saturated heterocycloalkyl in any case containing a total of 10 to 15 ring atoms, wherein A^1

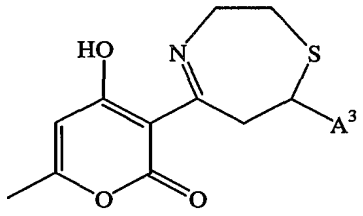
may be substituted with a group selected from $-R^3$, $-X^2OR^3$, $-X^2C(O)R^3$, $-X^2OC(O)R^3$, $-X^2C(O)OR^3$, $-X^2SR^3$, $-X^2S(O)R^3$, $-X^2S(O)_2R^3$, $-X^2NR^3R^4$, $-X^2NR^4C(O)R^3$, $-X^2NR^4C(O)OR^3$, $-X^2C(O)NR^3R^4$, $-X^2NR^4C(O)NR^3R^4$, $-X^2NR^4C(NR^4)NR^3R^4$, $-X^2NR^4S(O)_2R^3$ and $-X^2S(O)_2NR^3R^4$, wherein X^2 is a bond or (C_{1-6})alkylene, R^3 is $-X^2R^5$ wherein X^2 is as defined above and R^5 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, wherein each ring within A^1 and R^5 contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A^1 and R^5 may be substituted further with 1 to 2 groups independently selected from (C_{1-6})alkylidene, oxo, imino and thioxo, with the provisos that only one of A^1 and R^5 is a fused polycyclic ring system;

A^2 is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A^2 may be substituted with a group selected from $-R^8$, $-X^2OR^8$, $-X^2C(O)R^8$, $-X^2OC(O)R^8$, $-X^2C(O)OR^8$, $-X^2SR^8$, $-X^2S(O)R^8$, $-X^2S(O)_2R^8$, $-X^2NR^4R^8$, $-X^2NR^4C(O)R^8$, $-X^2NR^4C(O)OR^8$, $-X^2C(O)NR^4R^8$, $-X^2NR^4C(O)NR^4R^8$, $-X^2NR^4C(NR^4)NR^4R^8$, $-X^2NR^4S(O)_2R^8$ and $-X^2S(O)_2NR^4R^8$, wherein X^2 is a bond or (C_{1-6})alkylene, R^8 is $-X^2R^9$ wherein X^2 is as defined above and R^9 is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or

halo-substituted (C_{1-6})alkyl, wherein each ring within A^2 and R^8 contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2C(O)NR^4X^2C(O)OR^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A^2 and R^8 may be substituted further with 1 to 2 groups independently selected from (C_{1-6})alkylidene, oxo, imino and thioxo, with the proviso that only one of A^2 and R^8 is a fused polycyclic ring system; and

A^3 is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A^3 may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2C(O)R^9$, $-X^2OC(O)R^9$, $-X^2C(O)OR^9$, $-X^2SR^9$, $-X^2S(O)R^9$, $-X^2S(O)_2R^9$, $-X^2NR^4R^9$, $-X^2NR^4C(O)R^9$, $-X^2NR^4C(O)OR^9$, $-X^2C(O)NR^4R^9$, $-X^2NR^4C(O)NR^4R^9$, $-X^2NR^4C(NR^4)NR^4R^9$, $-X^2NR^4S(O)_2R^9$ and $-X^2S(O)_2NR^4R^9$, wherein X^2 is a bond or (C_{1-6})alkylene, R^9 is $-X^2R^{10}$ wherein X^2 is as defined above and R^{10} is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl, wherein each ring within A^3 and R^{10} contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, cyano, halo, nitro, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2C(O)R^6$, $-X^2OC(O)R^6$, $-X^2C(O)OR^4$, $-X^2SR^4$, $-X^2S(O)R^6$, $-X^2S(O)_2R^6$, $-X^2NR^4R^4$, $-X^2NR^4C(O)R^6$, $-X^2NR^4C(O)OR^4$, $-X^2C(O)NR^4R^4$, $-X^2NR^4C(O)NR^4R^4$, $-X^2NR^4C(NR^4)NR^4R^4$, $-X^2NR^4S(O)_2R^6$ and $-X^2S(O)_2NR^4R^4$, wherein X^2 and R^4 are as defined above and R^6 is (C_{1-6})alkyl or

halo-substituted (C_{1-6})alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A^3 and R^{10} may be substituted further with 1 to 2 groups independently selected from (C_{1-6})alkylidene, oxo, imino and thioxo, with the proviso that only one of A^3 and R^{10} is a fused polycyclic ring system; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.; with the proviso that when said compound is of Formula II(a):



II(a)

then A^3 is other than:

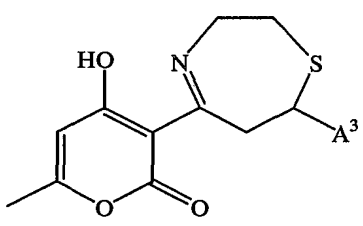
(a) benzo[1,3]dioxolyl;

(b) phenyl which is mono-substituted by bromo, hydroxy, methyl or isopropyl; and

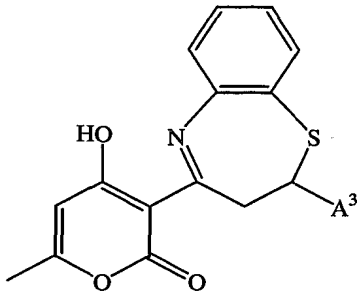
(c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

77. The method of claim 76, with the further proviso that when said compound is selected the group consisting of Formula II(a) and II(b):



II(a)



II(b)

then A^3 is other than:

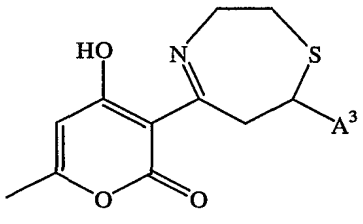
(a) benzo[1,3]dioxolyl;

(b) phenyl which is mono-substituted by bromo, nitro, hydroxy, methyl or isopropyl; and

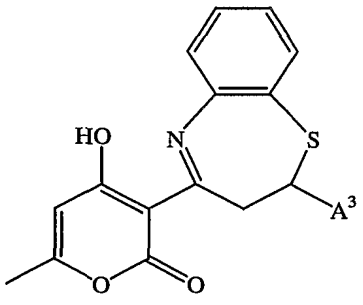
(c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

78. The method of claim 76, with the further proviso that when said compound is selected the group consisting of Formula II(a) and II(b):



II(a)



II(b)

then A^3 is other than:

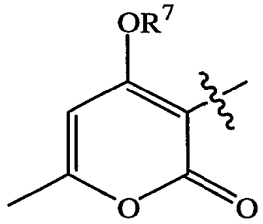
(a) benzo[1,3]dioxolyl;

(b) 2,3-dihydro-benzo[1,4]dioxinyl; and

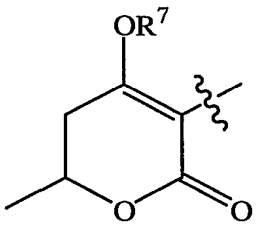
(c) phenyl which is substituted by at least one of bromo, chloro, hydroxy, nitro, methoxy and (C_{1-3})alky; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof. 1.

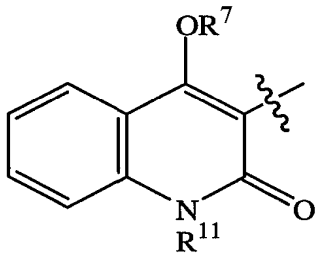
79. The method of Claim 76, wherein A^1 of said compound is a group selected from Formulae (a), (b), (c), (d) and (e):



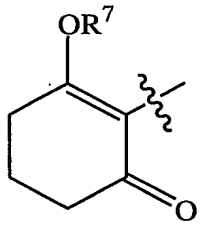
(a)



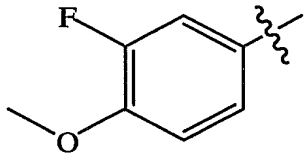
(b)



(c)



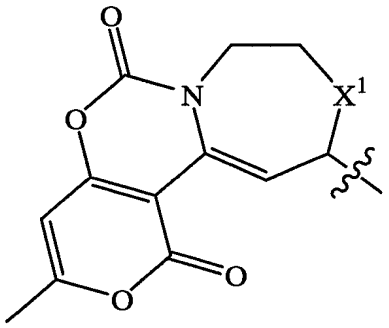
(d)



(e)

in which R^7 is hydrogen or methyl, R^{11} is hydrogen or (C_{1-6})alkyl and the free valance is attached to A^2, or

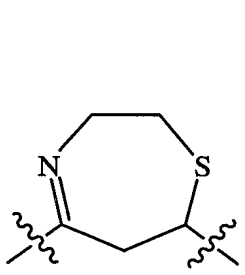
A^2 and A^1 together with R^1 and the atoms to which A^1 and R^1 are attached forms a group of Formula (g):



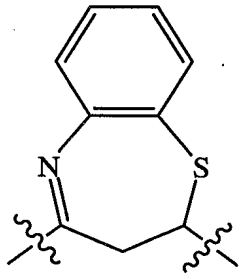
(g)

wherein X^1 is -S- and the free valance is attached to A^3; and

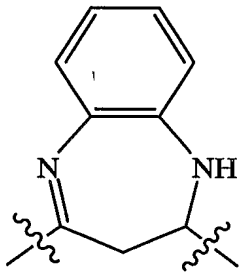
A^2 of said compound is as defined above or is a group selected from Formulae (h), (i), (j), (k), (l) and (m):



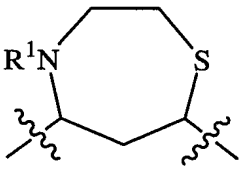
(h)



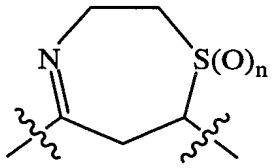
(i)



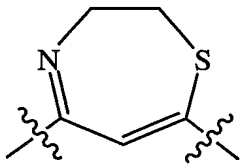
(j)



(k)



(l)



(m)

in which n is 1 or 2 and R^1 is acetyl or trifluoroacetyl; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

80. The method of Claim 79, wherein A^3 of said compound is phenyl or heteroaryl containing a total of 5 to 9 ring atoms, wherein A^3 may be substituted with a group selected from $-R^9$, $-X^2OR^9$, $-X^2SR^9$ and $-X^2S(O)_2R^9$,

wherein R^9 is $-X^2R^{10}$, X^2 is a bond or (C_{1-6})alkylene and R^{10} is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within A^3 and R^{10} may be substituted with 1 to 3 groups independently selected from (C_{1-6})alkyl, halo, halo-substituted (C_{1-6})alkyl, $-X^2OR^4$, $-X^2SR^4$, $-X^2S(O)_2R^6$ and $-X^2NR^4R^4$, wherein R^4 at each occurrence independently is hydrogen, (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl and R^6 is (C_{1-6})alkyl or halo-substituted (C_{1-6})alkyl; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

81. The method of Claim 80, wherein said compound is selected from the group consisting of:

4-hydroxy-3-[7-(2-methoxy-4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

2-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

4-hydroxy-3-[7-(4-methanesulfonyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

3-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

3-hydroxy-2-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-cyclohex-2-enone;

3-hydroxy-2-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone;

4-hydroxy-6-methyl-3-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-5,6-dihydro-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-5,6-dihydro-pyran-2-one; and

3-[7-(2,4-dimethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

82. The method of claim 76, wherein said compound is selected from the list consisting of:

3-[4-acetyl-7-(2,4-dimethoxy-phenyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-4-(2,2,2-trifluoro-ethanoyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

1-[7-(2,4-dimethoxy-phenyl)-5-(3-fluoro-4-methoxyphenyl)-[1,4]thizepan-4-yl]-ethanone;

4-hydroxy-6-methyl-3-[7-(3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-ethyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3[7-(2-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(3-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(4-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-[3-(3-trifluoromethyl-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-[3-(3,4-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-[3-(3,5-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(3-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-{7-[5-(2-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(3-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(4-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(2-chloro-5-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-[7-(4-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzenesulfonyl-1*H*-pyrrol-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(3-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(1-methyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3-chloro-2-methyl-5-trifluoromethyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(2,4-difluoro-benzenesulfonyl)-1*H*-pyrrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-(7-[2,2′]bithienyl-5-yl-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(3,5-dichloro-phenyl)-1*H*-pyrrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(4-chloro-phenyl)-1*H*-pyrrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-chloro-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(6-*p*-tolylsulfanyl-imidazo[2,1-*b*]thiazol-5-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4,5-dibromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2-chloro-5-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methylsulfanyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-chloro-1-methyl-3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[4-(2,4-dimethoxy-phenyl)-4,5-dihydro-3*H*-benzo[*b*][1,4]diazepin-2-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-2,4-dimethoxy-phenyl)-2,3,6,,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-1*H*-quinolin-2-one;

4-hydroxy-6-methyl-3-[7-(4-trifluoromethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-hydroxy-2-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone;

3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1*H*-1λ^4-[1,4]thiazepin-5-yl]-4-hydroxy-6-methoxy-pyran-2-one;

10-(2,4-dimethoxy-phenyl)-3-methyl-7,8-dihydro-10*H*-2,5-dioxa-9-thia-6a-aza-cyclohepta[*a*]naphthalene-1,6-dione;

3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3,6,7-tetrahydro-1*H*-1λ^6-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-(7-[2,2′]bithienyl-5-yl-2,3-dihydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone; and

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

83. A method for the treatment of drug resistant cancer, comprising administering to an animal in need of such treatment an effective amount of a compound selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4-ethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(3-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

3-[7-(2-bromo-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,3-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]4-hydroxy-6-methyl-pyran-2-one;

3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

6-methyl-3-(2-*p*-tolyl-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl)-pyran-2-one;

4-hydroxy-6-methyl-3-[2-(4-methylsulfanyl-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-pyran-2-one;

4-hydroxy-3-[7-(4-chloro-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; and

4-hydroxy-3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

84. The method of claim 83, wherein said compound is selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; and

6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

85. The method of Claim 66, 73, 76 or 83, further comprising administering to said animal at least one known cancer chemotherapeutic agent, or a pharmaceutically acceptable salt of said agent.

86. The method of Claim 85, wherein said known cancer therapeutic agent is selected from the group consisting of busulfan, cis-platin, mitomycin C, carboplatin, colchicine, vinblastine, paclitaxel, docetaxel, camptothecin, topotecan, doxorubicin, etoposide, 5-azacytidine, 5-fluorouracil, methotrexate, 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea, thioguanine, melphalan, chlorambucil, cyclophosamide, ifosfamide, vincristine, mitoguazone, epirubicin, aclarubicin, bleomycin, imitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen, Herceptin, Rituxan and alanosine.

87. The method of Claim 66, 73, 75 or 83, further comprising treating said animal with radiation-therapy.

88. The method of Claim 66, 73, 76 or 83, wherein said compound is administered after surgical treatment for cancer.

89. The method of Claim 57, wherein said disorder is an autoimmune disease.

90. The method of Claim 57, wherein said disorder is rheumatoid arthritis.

91. The method of Claim 57, wherein said disorder is inflammation or inflammatory bowel disease.

92. The method of Claim 57, wherein said disorder is psoriasis.

93. The method of Claim 57, wherein said disorder is a skin disease.